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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.												
10/717,196	11/19/2003	Morten Eriksen	NIDN-10378	6245												
7590 Amersham Health, Inc. 101 Carnegie Center Princeton, NJ 08540		07/16/2007	<table border="1"><tr><td colspan="2">EXAMINER</td></tr><tr><td colspan="2">SCHLIENTZ, LEAH H</td></tr><tr><td>ART UNIT</td><td>PAPER NUMBER</td></tr><tr><td>1618</td><td></td></tr><tr><td>MAIL DATE</td><td>DELIVERY MODE</td></tr><tr><td>07/16/2007</td><td>PAPER</td></tr></table>		EXAMINER		SCHLIENTZ, LEAH H		ART UNIT	PAPER NUMBER	1618		MAIL DATE	DELIVERY MODE	07/16/2007	PAPER
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	Application No. 10/717,196	Applicant(s) ERIKSEN ET AL.	
	Examiner Leah Schlientz	Art Unit 1618	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --  
**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

#### Status

- 1) ☒ Responsive to communication(s) filed on 4/30/07.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

#### Disposition of Claims

- 4) ☒ Claim(s) 1-17 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 1-17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

#### Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

#### Priority under 35 U.S.C. § 119

- 12) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☒ Certified copies of the priority documents have been received in Application No. 09/693,836.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

#### Attachment(s)

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)  | 4) <input type="checkbox"/> Interview Summary (PTO-413)<br>Paper No(s)/Mail Date. _____ |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)   | 5) <input type="checkbox"/> Notice of Informal Patent Application                       |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)<br>Paper No(s)/Mail Date <u>3/25/04</u> . | 6) <input type="checkbox"/> Other: _____  |

## DETAILED ACTION

### *Election/Restrictions*

The election without traverse of the following species, in the reply filed 4/30/2007, is acknowledged: Example 7, which includes a combination of Preparation 1 and Preparation 9. Said election corresponds to i) perfluorobutane as the dispersed gas and phosphatidylserine as the material serving to stabilize said gas in the first composition and ii) perfluoromethylcyclopentane as the diffusible component and phosphatidylcholine as the material to stabilize the emulsion in the second composition. Claims 1 – 17 are pending. All currently pending claims are readable upon the elected species.

### *Double Patenting*

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., *In re Berg*, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 – 17 are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 – 18 of U.S. Patent No. 6,375,931, in view of Klaveness *et al.* (US 6,110,444). Although the conflicting claims are not identical, they are not patentably distinct from each other both sets of claims are drawn to a combined preparation for simultaneous, separate or sequential use as a contrast agent in ultrasound imaging comprising a first composition comprising i) an injectable aqueous medium having gas dispersed therein and ii) an composition comprising a diffusible component capable of diffusing into the dispersed gas. The compositions further comprise stabilizing materials including surfactants, protein, polymer, phospholipids, etc. While the claims of the '931 patent do not specifically require that the stabilizing materials to have opposite charges from one another, it would have been obvious to one of ordinary skill in the art to practice the instant claims when in possession of the patented claims because Klaveness teaches that it is known in the art to use one or more surfactants to promote additional stabilization of microbubbles. For example, two polymers or macromolecules of opposite charge upon mixing will form a polyelectrolyte complex with low solubility in water, leading to coacervation and formation of a protective microencapsulating layer around microbubbles (column 4, lines 21 – 65).

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

The factual inquiries set forth in *Graham v. John Deere Co.*, 383 U.S. 1, 148 USPQ 459 (1966), that are applied for establishing a background for determining obviousness under 35 U.S.C. 103(a) are summarized as follows:

1. Determining the scope and contents of the prior art.
2. Ascertaining the differences between the prior art and the claims at issue.
3. Resolving the level of ordinary skill in the pertinent art.
4. Considering objective evidence present in the application indicating obviousness or nonobviousness.

Claims 1 – 17 are rejected under 35 U.S.C. 103(a) as being unpatentable over Unger (WO 97/40858) and Lohrmann (US 5,716,597), in view of Schutt (US 5,605,673), in further view of Klaveness *et al.* (US 6,110,444).

Unger teaches contrast agents employed in ultrasound comprising a microsphere filled with a fluorine-containing gas, such as pefluoropentane, perfluorobutane, perfluorohexane, perfluoropropane and a phospholipids, see pages 11 – 14, claims 1 – 5. Unger further teaches that negatively charged lipids lend enhanced stability to the microspheres (page 15, lines 18 – 34). Unger teaches the total concentration of lipids in the lyophilized lipid composition is at least 50%, more preferably 80% or 90% (page 16,

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lines 16 – 28). Unger does not teach a second perfluorocarbon as a dispersible component.

Lohrmann teaches an ultrasonic imaging agent comprising an oil-in-water emulsion of a gas-forming chemical (i.e. perfluorobutane) and a stabilizer (e.g. phospholipids) (abstract; column 2, line 39 – column 3, line 4; column 4, lines 26 – 50). Lohrmann further teaches that the stabilizer may be used singly or in various combinations in the emulsions as in the emulsions of the present invention (see column 5, lines 6 – 7). Lohrmann teach a variety of stabilizers, including phosphatidylcholine, phosphatidylserine, etc. (column 4, lines 47 – 48) and that the stabilizer may be used singly or in various combination in the emulsions (column 5, line 6). As in Unger, Lohrmann does not use a second perfluorocarbon as a dispersible component.

Schutt teaches ultrasonic contrast agents comprising microbubbles encapsulating a first and a second perfluorocarbon gas in combination with or without an osmotic gas (abstract and column 14 – 18). Schutt further claims that such gases may be a combination of perfluorobutane and perfluormethylcyclopentane (See Table 1, claims 43 and 54). See also claims 29 and 82, wherein Schutt clearly sets forth that a secondary osmotic gas can be a perfluorocarbon including perfluorohexane or trichlorofluoroethane (Freon 113). Therefore, liquid perfluorocarbons including perfluoromethylcyclopentane, for example, are viewed to act as art equivalents in ultrasound contrast agents.

Klaveness teaches the use one or more surfactants to promote additional stabilization of microbubbles. For example, two polymers or macromolecules of

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opposite charge upon mixing will form a polyelectrolyte complex with low solubility in water, leading to coacervation and formation of a protective microencapsulating layer around microbubbles (column 4, lines 21 – 65).

Accordingly, it would have been obvious to one of ordinary skill in the art at the time of the instant invention to combine the compositions of Unger or Lohrmann with those of Schutt, because as reasoned by Schutt, two perfluorocarbon moieties can be combined with one another and that a secondary liquid perfluorocarbon moiety can enhance the stability of the microbubble during ultrasound imaging. An artisan of ordinary skill would have had a reasonable expectation of success in doing so, because liquid perfluorocarbons are expected to act as equivalents in ultrasound contrast agents, and thus substitution of perfluoromethylcyclopentane in place of perfluorohexane would have been an obvious modification. It would have been further obvious to include stabilizing materials having opposite charges in the compositions because Klaveness specifically teaches that such practice leads to coacervation and formation of a protective microencapsulating layer around microbubbles.

### ***Conclusion***

No claims are allowed at this time.


Any inquiry concerning this communication or earlier communications from the examiner should be directed to Leah Schlientz whose telephone number is 571-272-9928. The examiner can normally be reached on Monday - Friday 8 AM - 5 PM.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Michael Hartley can be reached on 571-272-0616. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

LHS



SREENI PADMANABHAN  
SUPERVISORY PATENT EXAMINER